

WHAT IS CLAIMED IS:

1. An isolated protein complex comprising two proteins, the protein complex selected from the group consisting of

- (a) a complex set forth in Table 1;
- (b) a complex set forth in Table 2;
- (c) a complex set forth in Table 3;
- (d) a complex set forth in Table 4;
- (e) a complex set forth in Table 5;
- (f) a complex set forth in Table 6;
- (g) a complex set forth in Table 7;
- (h) a complex set forth in Table 8;
- (i) a complex set forth in Table 9;
- (j) a complex set forth in Table 10;
- (k) a complex set forth in Table 11;
- (l) a complex set forth in Table 12;
- (m) a complex set forth in Table 13;
- (n) a complex set forth in Table 14;
- (o) a complex set forth in Table 15;
- (p) a complex set forth in Table 16;
- (q) a complex set forth in Table 17;
- (r) a complex set forth in Table 18;
- (s) a complex set forth in Table 19;
- (t) a complex set forth in Table 20;
- (u) a complex set forth in Table 21;
- (v) a complex set forth in Table 22;
- (w) a complex set forth in Table 23;
- (x) a complex set forth in Table 24;
- (y) a complex set forth in Table 25;
- (z) a complex set forth in Table 26;
- (aa) a complex set forth in Table 27;
- (ab) a complex set forth in Table 28;

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(ac) a complex set forth in Table 29;

(ad) a complex set forth in Table 30;

(ae) a complex set forth in Table 31;

(af) a complex set forth in Table 32;

5 (ag) a complex set forth in Table 33;

(ah) a complex set forth in Table 34;

(ai) a complex set forth in Table 35;

(aj) a complex set forth in Table 36;

(ak) a complex set forth in Table 37;

10 (al) a complex set forth in Table 38;

(am) a complex set forth in Table 39;

(an) a complex set forth in Table 40;

(ao) a complex set forth in Table 41;

(ap) a complex set forth in Table 42;

15 (aq) a complex set forth in Table 43;

(ar) a complex set forth in Table 44;

(as) a complex set forth in Table 45

(at) a complex set forth in Table 46;

(au) a complex set forth in Table 47;

20 (av) a complex set forth in Table 48;

(aw) a complex set forth in Table 49;

(ax) a complex set forth in Table 50;

(ay) a complex set forth in Table 51;

(az) a complex set forth in Table 52;

25 (ba) a complex set forth in Table 53;

(bb) a complex set forth in Table 54;

(bc) a complex set forth in Table 55;

(bd) a complex set forth in Table 56;

(be) a complex set forth in Table 57;

30 (bf) a complex set forth in Table 58;

(bg) a complex set forth in Table 59;

(bh) a complex set forth in Table 60;

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(bi) a complex set forth in Table 61;
 (bj) a complex set forth in Table 62;
 (bk) a complex set forth in Table 63;
 (bl) a complex set forth in Table 64;
 5 (bm) a complex set forth in Table 65;
 (bn) a complex set forth in Table 66;
 (bo) a complex set forth in Table 67;
 (bp) a complex set forth in Table 68;
 (bq) a complex set forth in Table 69;
 10 (br) a complex set forth in Table 70;
 (bs) a complex set forth in Table 71;
 (bt) a complex set forth in Table 72; and
 (bu) a complex set forth in Table 73.

15 2. The protein complex of claim 1, wherein said protein complex comprises complete proteins.

3. The protein complex of claim 1, wherein said protein complex comprises a fragment of one
 20 protein and a complete protein of another protein.

4. The protein complex of claim 1, wherein said protein complex comprises fragments of
 proteins.

5. An isolated antibody selectively immunoreactive with the protein complex of claim 1.

25 6. The antibody of claim 5, wherein said antibody is a monoclonal antibody.

7. A method for diagnosing a physiological disorder in an animal, which comprises assaying
 for:

(a) whether a protein complex set forth in any one of Tables 1-73 is present in a
 30 tissue extract;

(b) the ability of proteins to form a protein complex set forth in any one of Tables
 1-73; and

(c) a mutation in a gene encoding a protein of a protein complex set forth in any one of Tables 1-73.

8. The method of claim 7, wherein said animal is a human.

9. The method of claim 7, wherein the diagnosis is for a predisposition to said physiological disorder.

10. The method of ~~claim~~ 7, wherein the diagnosis is for the existence of said physiological disorder.

11. The method of claim 7, wherein said assay comprises a yeast two-hybrid assay.

12. The method of claim 7, wherein said assay comprises measuring *in vitro* a complex formed by combining the proteins of the protein complex, said proteins isolated from said animal.

13. The method of claim 12, wherein said complex is measured by binding with an antibody specific for said complex.

14. The method of claim 7, wherein said assay comprises mixing an antibody specific for said protein complex with a tissue extract from said animal and measuring the binding of said antibody.

15. A method for determining whether a mutation in a gene encoding one of the proteins of a protein complex set forth in any one of Tables 1-73 is useful for diagnosing a physiological disorder, which comprises assaying for the ability of said protein with said mutation to form a complex with the other protein of said protein complex, wherein an inability to form said complex is indicative of said mutation being useful for diagnosing a physiological disorder.

16. The method of claim 15, wherein said gene is an animal gene.

17. The method of claim 16, wherein said animal is a human.

18. The method of claim 15, wherein the diagnosis is for a predisposition to a physiological disorder.

5 19. The method of claim 15, wherein the diagnosis is for the existence of a physiological disorder.

20. The method of claim 15, wherein said assay comprises a yeast two-hybrid assay.

10 21. The method of claim 15, wherein said assay comprises measuring *in vitro* a complex formed by combining the proteins of the protein complex, said proteins isolated from an animal.

22. The method of claim 21, wherein said animal is a human.

15 23. The method of claim 21, wherein said complex is measured by binding with an antibody specific for said complex.

20 ~~24.~~ A method for screening for drug candidates capable of modulating the interaction of the proteins of a protein complex set forth in any one of Tables 1-73, which comprises:

(a) combining the proteins of said protein complex in the presence of a drug to form a first complex;

(b) combining the proteins in the absence of said drug to form a second complex;

(c) measuring the amount of said first complex and said second complex; and

25 (d) comparing the amount of said first complex with the amount of said second complex,

wherein if the amount of said first complex is greater than, or less than the amount of said second complex, then the drug is a drug candidate for modulating the interaction of the proteins of said protein complex. ~~X~~

30 25. The method of claim 24, wherein said screening is an *in vitro* screening.

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26. The method of claim 24, wherein said complex is measured by binding with an antibody specific for said protein complexes.

27. The method of claim 24, wherein if the amount of said first complex is greater than the amount of said second complex, then said drug is a drug candidate for promoting the interaction of said proteins.

28. The method of claim 24, wherein if the amount of said first complex is less than the amount of said second complex, then said drug is a drug candidate for inhibiting the interaction of said proteins.

~~29.~~ A non-human animal model for a physiological disorder wherein the genome of said animal or an ancestor thereof has been modified such that the formation of a protein complex set forth in any one of Tables 1-73 has been altered.

~~30.~~ The non-human animal model of claim 29, wherein the formation of said protein complex has been altered as a result of:

- (a) over-expression of at least one of the proteins of said protein complex;
- (b) replacement of a gene for at least one of the proteins of said protein complex with a gene from a second animal and expression of said protein;
- (c) expression of a mutant form of at least one of the proteins of said protein complex;
- (d) a lack of expression of at least one of the proteins of said protein complex; or
- (e) reduced expression of at least one of the proteins of said protein complex.

31. A cell line obtained from the animal model of claim 29.

~~32.~~ A non-human animal model for a physiological disorder, wherein the biological activity of a protein complex set forth in any one of Tables 1-73 has been altered.

33. The non-human animal model of claim 32, wherein said biological activity has been altered as a result of:

- (a) disrupting the formation of said complex; or
- (b) disrupting the action of said complex.

34. The non-human animal model of claim 32, wherein the formation of said complex is
5 disrupted by binding an antibody to at least one of the proteins which form said protein
complex.

35. The non-human animal model of claim 32, wherein the action of said complex is disrupted
by binding an antibody to said complex.

36. The non-human animal model of claim 32, wherein the formation of said complex is
disrupted by binding a small molecule to at least one of the proteins which form said protein
complex.

37. The non-human animal model of claim 32, wherein the action of said complex is disrupted
by binding a small molecule to said complex.

38. A cell in which the genome of cells of said cell line has been modified to produce at least
one protein complex set forth in any one of Tables 1-73.

39. A cell line in which the genome of the cells of said cell line has been modified to eliminate
at least one protein of a protein complex set forth in any one of Tables 1-73.

40. A method of screening for drug candidates useful in treating a physiological disorder
which comprises the steps of:

- (a) measuring the activity of a protein selected from the proteins set forth in Tables
1-73 in the presence of a drug,
- (b) measuring the activity of said protein in the absence of said drug, and
- (c) comparing the activity measured in steps (1) and (2),

wherein if there is a difference in activity, then said drug is a drug candidate for treating
said physiological disorder.

41. An isolated nucleic acid encoding a polypeptide comprising an amino acid sequence selected from the group consisting of amino acid sequences set forth in SEQ ID NOs:4, 6, 8 and 10.

42. The isolated nucleic acid of claim 41 comprising a nucleotide sequence selected from the group consisting of nucleotide sequences set forth in SEQ ID NOs:3, 5, 7 and 9.

43. An isolated polypeptide comprising an amino acid amino acid sequence selected from the group consisting of amino acid sequences set forth in SEQ ID NOs:4, 6, 8 and 10.

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